

REMARKS

With the cancellation of claim 33 and the addition of claim 42, claims 1-12, 25-28, 30, 32 and 36-41 are pending.

Support for the new claim 42 can be found in the specification at page 18, line 22 to page 19, line 11, and Figure 1.

Claim Rejections - 35 U.S.C. 112, Second Paragraph

Claims 1-3, 25-28, 30, 32, 33 and 35-41 were rejected as being indefinite under 35 U.S.C. 112, second paragraph, because of the word “obtained”. Applicants respectfully traverse the rejection. The recitation with the word “obtained” in these claims means that the origin of the thermostable DNA polymerase to be modified is from the *Pyrococcus* or *Thermococcus* genus.

Claim 33 was further rejected as indefinite because of the term “thermostable.” Applicants respectfully disagree with the rejection. However, to advance prosecution, claim 33 has been cancelled.

Withdrawal of the indefiniteness rejections is requested.

Claim Rejections - 35 U.S.C. 112, First Paragraph

Claims 1-12, 25-28, 30, 32, 33 and 36-41 were rejected as failing the written description requirement because the Office Action alleges that there was no support for a modified thermostable DNA polymerase obtained from *Pyrococcus* or *Thermococcus* genus with the replacement of histidine by another amino acid in the DIETLYH or DIETFYH sequence within the exonuclease I region. Applicants respectfully traverse the rejections.

The Office Action asserts that the specification only provides representative species from *Pyrococcus furiosus*, *Pyrococcus kodakaraensis* KOD1 and *Thermococcus litoralis*. Applicants respectfully disagree because page 18, line 22 to page 19, line 11, of the specification discloses the modified thermostable DNA polymerase having the DX₁EX₂X₃X₄H amino acid sequence in the EXO I region, with the replacement of the histidine residue in the DX₁EX₂X₃X₄H amino acid sequence with another amino acid. In particular, the attention of the Examiner is drawn to page 19, lines 10-11, which specifically states that there is no restriction on the origin of the thermostable DNA polymerase having DX₁EX₂X₃X₄H amino acid sequence. Since there is no restriction on the origin of the thermostable DNA polymerase before modification, and since page 19, lines 14-18, also discloses *Pyrococcus furiosus*, *Pyrococcus kodakaraensis* KOD1 and *Thermococcus litoralis* as examples of the sources of the thermostable DNA polymerase having

the DX₁EX₂X₃X₄H amino acid sequence, applicants submit that there is descriptive support for the *Pyrococcus* or *Thermococcus* genus as the origin of the thermostable DNA polymerase for the modified thermostable DNA polymerase claimed in claims 1-12, 25-28, 30, 32, 33 and 36-41.

Page 2, lines 4-5, of the specification discloses that there are α -like DNA polymerases such as thermostable DNA polymerases derived from *Pyrococcus furiosus*, *Pyrococcus kodakaraensis* KOD1 and *Thermococcus litoralis*. In Fig. 1, the terms “(*Pyrococcus*)” after KOD and Pfu and “(*Thermococcus*)” after Vent as examples of the hyperthermophilic archaeon-derived thermostable DNA polymerase also provide descriptive support for the *Pyrococcus* or *Thermococcus* genus as the origin of the thermostable DNA polymerase for the modified thermostable DNA polymerase claimed.

Hashimoto et al. (J. Mol. Biol. (2001) 306:469-477), and Rodriguez et al. (J. Mol. Biol. (2000) 299: 447-462), cited in the attached IDS describe various species belonging to the *Pyrococcus* and *Thermococcus* genera, including *Pyrococcus kodakaraensis* KOD1 and *Thermococcus* sp. 9°N-7 as archaea.

At the time of the filing of the instant application, the crystal structures of DNA polymerases derived from the *Pyrococcus* and *Thermococcus* genera were shown in the literature to be essentially identical. More specifically, the crystal structures of DNA polymerases, for example, Tgo derived from *Thermococcus* (Hopfner et al., Proc. Nat'l Acad. Sci. (1999) 96:3600-3605, cited in the IDS), 9°N-7 derived from *Thermococcus* (Rodriguez et al.) and KOD1 derived from *Thermococcus* (previously classified as *Pyrococcus*) (Hashimoto et al.) were analyzed and known to be structurally identical (see page 470, right column, lines 14-17, Hashimoto et al.). In page 291, lines 4-5, of Kuroita et al. (J. Mol. Biol. (2005), 351:291-298, cited in the IDS attached), it was disclosed that KOD1 used to be classified as a polymerase from the *Pyrococcus* genus, but KOD1 is now classified in the *Thermococcus* genus.

Applicants hereby submit a chart showing the homology of the amino acid sequences of Pfu and KOD1, with the sequence of Pfu taken from Uemori et al. (Nucleic Acid Research (1993) 21:259-265, cited in the IDS attached) and the sequence of KOD1 taken from SEQ ID NO:1 in JP No. 1995-298879 (cited in the IDS attached). In the alignment, identical amino acids are indicated by an “*”, and similar amino acids are indicated by “.”. The alignment reveals 79.8% identity between the amino acid sequences of Pfu and KOD1, and most of the amino acids not

identical are chemically similar. Therefore, the amino acid sequences of Pfu and KOD1 are highly conserved.

Thus, as shown by the above facts, the *Pyrococcus* and *Thermococcus* genera are very similar.

With the descriptive support in the specification and drawings, applicants submit that the phrase “*Pyrococcus* or *Thermococcus* genus” in claim 1 does not raise new issue and does meet the written description requirement. Withdrawal of the written description rejections is requested.

Conclusion

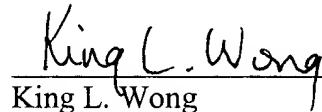
In light of the above reasoning, applicants submit that the application is in a condition for allowance. A Notice of Allowance is believed in order.

In the event that the filing of this paper is deemed not timely, applicants petition for an appropriate extension of time. The petition fee, and any other fees that may be required in relation to the filing of this paper, can be charged to Deposit Account No. 11-0600, referencing Docket No. 10089/14.

Respectfully Submitted,

KENYON & KENYON LLP

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Attachments: Petition for Extension of Time;
IDS
Amino Acid Sequence Homology Data (2 pgs.)

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